REMARKS

Claims 85 and 86 are pending in the application.

- Claims 85 and 86 are rejected under 35 USC 112, second paragraph (indefiniteness).
- Claims 85 and 86 are rejected under 35 USC 112, second paragraph (enablement).
- Claims 85 and 86 are rejected under 35 USC 102(b).

Rejection under USC 35, 112, second paragraph (Indefiniteness)

The Examiner has rejected Claims 85 and 86 as not being indefinite for failing to particularly point out and directly claim the subject matter which applicant regards as his invention. Specifically, the Examiner states:

> The Claim recites "physiological levels" of albumin, however, the specification does not clearly define what concentration range is considered physiological. Action dated 7/31/2007, page 2.

Applicant respectfully traverses the rejection. This phrase was rejected in an Office Action dated 3/13/2006 under 35, 112, first paragraph (enablement) and addressed by Applicant in the Response dated 7/25/2006. Examiner acknowledged that the rejection was overcome and the claims enabled in view of Applicant's arguments in the Action dated 11/30/2006.

In regards to indefiniteness, the MPEP states:

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP 2173.02.

Attached as Exhibit A is a description of a research project on the website of the Australian Proteome Analysis Facility (APAF Ltd), Australia's premier proteomics institution. According to their website, APAF Ltd was the birthplace of the term proteomics in 1995 and the first high throughput lab worldwide. APAF research and development has continued in all areas of technology development and industry, providing world leading advances and services for over a decade. The research project described relates to a novel cyclic immunodepletion technique for the removal of highly abundant proteins in human plasma, thereby enabling the

study of low abundant protein markers present in plasma. The second paragraph of the description of the research project indicates that albumin is present at levels of approximately 60 mg/ml. It is respectfully submitted that the term "physiological levels" of albumin were known in the art at the time of the present invention and that the term is definite based on the knowledge in the art at the time of the invention. Applicant also submits that above-stated rejection has been adequately addressed and withdrawal of the rejection is requested.

Examiner further contends that steps are missing from the Claims as pending. In particular, Examiner states the Claims are "incomplete for omitting essential steps." Examiner arrives at this conclusion by defining the invention as being drawn to *in* vivo use only.

The Claims, as drafted, are directed towards a method of forming an immune complex between beta-amyloid and an antibody specific for a beta-amyloid epitope in the presence of physiological levels of human serum albumin or in the presence of up to 60 mg/ml human serum albumin. The Claims, as drafted, are not intended to be limited to an *in vivo* method. Thus, Examiner's request for additional steps directed towards, for example, the administration of the antibody is inappropriate. Additionally and contrary to Examiner's assertion, the Claims, as drafted define the result or effect of the method claimed with that being "the binding of antibody to antigen." However and without acquiescing to the Examiner's arguments and solely to advance the business interests of the Applicant and while reserving the right to prosecute the unamended or similar claim in the future, Applicant has amended Claims 85 and 86 to recite a detection step. Support for this amendment can be found in the subject specification at paragraph [0075] and Table 3 for *in vitro* use as well as at paragraph [0088] and Table 7 for *in vivo* use. Thus, Applicant respectfully requests that the rejection be withdrawn.

Examiner further contends that the Claims read on "beta-amyloid that is typically present in humans in the physiological state" and read "upon the Aβ autoimmune antibodies that are known in the art to be present in the native state." Examiner then suggests that the claims, as pending, may be directed towards non-statutory subject mater.

Although a rejection has not been made, Applicant replies. Applicant notes that Examiner's claim that Aβ autoimmune antibodies are known in the art is unsupported in the pending Action. However and without acquiescing to the Examiner's arguments and solely to advance the business interests of the Applicant and while reserving the right to prosecute the unamended or similar claim in the future, Applicant has amended Claims 85 and 86 to recite a detection step. Support for this amendment can be found in the subject specification at

paragraph [0075] and Table 3 for *in vitro* use as well as at paragraph [0088] and Table 7 for *in vivo* use. Thus, Applicant respectfully requests that the rejection be withdrawn.

Rejection under USC 35, 112, first paragraph (Enablement)

The Examiner has rejected Claims 85 and 86 as containing subject matter that is not described in the specification in such a way as to enable one skilled in the art to which it pertains. In particular, the Examiner states:

> ... the specification, while being enabling for an *in vitro* method of forming an immune complex comprising contacting beta-amyloid with a specific antibody in the present of human serum albumin, does not reasonably provide enablement for the method practiced *in vivo*. Office Action mailed 7/31/2007, page 4.

In particular, Examiner states, "Examiner does not argue that one of ordinary skill in the art would be able to readily practice these steps *in vitro*. However, Applicant fails to provide guidance as to how the method is to be practiced *in vivo*." Office Action mailed 7/31/2007, page 5.

Specification is Enabling for Practice of the Invention *in vivo*

Applicant respectfully traverses the rejection and submits that the specification as filed provides support for the practice of the present invention *in vivo*. Examiner's attention is directed towards paragraphs [0087], [0088] and Table 7 of the pending specification wherein an *in vivo* use of the presently claimed invention is taught. In this example, a murine model system is used to demonstrate that an antibody specific for an epitope of beta-amyloid forms an immune complex with beta-amyloid in the presence of physiological levels of serum albumin. Animal model systems are acceptable support for a method if the animal model system is accepted in the art as correlating with the claimed method of the invention. MPEP 2104.02. A rigorous correlation is not required.

> [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.). *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985)

And, "Since the initial burden is on the Examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example." MPEP 2164.02. Examiner has failed to provide any such reasons in

this or any prior Action. Therefore, Applicant submits that the specification as filed provides support for the pending claims as amended and respectfully requests that the rejection be withdrawn.

Rejection under USC 35, 102(b)

Examiner has rejected Claims 85 and 86 under USC 35, 102(b) as being anticipated by Biere, *et al.* Applicant respectfully disagrees.

In order for a reference to be anticipatory the reference must teach every element of the claimed invention. MPEP 2131. Examiner states that the cited reference teaches that ~89 % of beta-amyloid is bound to albumin. Examiner states that the cited article teaches running the beta-amyloid:albumin complex on a non-denaturing gel and then performing a Western blot assay with anti-beta-amyloid antibody. Importantly, however, the cited reference makes no teaching of the concentration of albumin in the context of the Western blot assay where the immune complex between beta-amyloid and an anti-beta-amyloid antibody is formed.

Examiner continues by stating the Biere, *et al.*, teaches that "such an immune complex can form in the presence of physiological concentrations of albumin as defined as nanomolar concentrations (pg. 32916, last paragraph)." However, Examiner mischaracterizes the reference. The reference teaches the beta-amyloid, "when incubated in fresh human plasma at physiological (nanomolar) concentrations bind to certain plasma proteins [*i. e.*, albumin]." The cited reference does not teach the formation of an immune complex between beta-amyloid and an antibody specific fro a beta-amyloid epitope in the presence of physiological levels of human serum albumin or in the presence of up to 60 mg/ml human serum albumin, as is claimed in the present invention.

It is extremely unlikely that the concentration of serum albumin in the context a Western blot assay is the same as in the physiological state. Since concentration is a function of volume, one would need to extrapolate the concentration of albumin in the context of the Western blot based on the albumin present in the volume of solution present at the point of interaction between the antigen and antibody. Examiner did not do this. Examiner **can not** avoid the legal requirement for anticipation of having the reference teach every element of the invention by merely stating: "barring evidence to the contrary" the cited reference teaches a limitation of the claim. That the Examiner could not point to this claim element in the reference either expressly or inherently is taken as an admission by the Examiner that the cited reference is not anticipatory of the pending claimed invention. As such, Applicant requests the withdrawal of the rejection.

Summary

In light of the above Response, the passing of the subject patent application to allowance is respectfully requested.

Respectfully submitted,

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Portsmouth, NH
Date: 6/6/08